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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
FORMAN, BETTY J	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 04/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/735,099	DAPPRICH ET AL.	
	Examiner	Art Unit	
	BJ Forman	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-19,21 and 39-55* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-19,21 and 39-55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 15 January 2004 has been entered.

Status of the Claims

2. This action is in response to papers filed 15 January 2004 in which claims 1, 3-5, 7, 9-11, 18-19 were amended and claims 39-55 were added. All of the amendments have been thoroughly reviewed and entered. The previous rejections in the Office Action dated 12 December 2002 are withdrawn in view of the amendments. All of the arguments have been thoroughly reviewed and are discussed below as they apply to the new grounds for rejection. New grounds for rejection are discussed.

Claims 1, 3-19, 21 and 39-55 are under prosecution.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The instant claims are drawn to a method for separating a polynucleotide molecule from a population of nucleic acids. The polynucleotide molecule includes a target nucleic acid sequence within 100 nucleotides of a distinguishing element.

While limitations from the specification are not drawn into the claims, the claims are interpreted in light of the specification. The specification defines the claimed population as "any population of nucleic acids" including amplified DNA (page 2, lines 20-24) and defines the claimed distinguishing element as "any sequence of interest" (page 3, lines 8-9). As such, the claimed distinguishing element can be interpreted as being any sequence within or within 100 nucleotides of the target sequence.

4. Claims 1, 3-13, 17, 18, 39-46 are rejected under 35 U.S.C. 102(a) and (e) as being anticipated by Ju et al (U.S. Patent No. 5,876,936, issued 2 March 1999).

Regarding Claim 1, Ju et al disclose a method for separating a polynucleotide molecule from a population comprising providing a population of nucleic acid molecules (i.e. mixture of differently sized primer extension products, Column 6, lines 13-47) comprising the polynucleotide having a first target sequence within 100 nucleotides of a distinguishing element (primer binding site adjacent to site of terminator incorporation, Column 5, lines 11-13), contacting the population of nucleic acid molecules with a first targeting element (i.e. primer) which specifically binds to the polynucleotide molecule, selectively attaching a separation group (biotinylated ddNTP) to the targeting element bound to the polynucleotide wherein the attaching only occurs when the primer is bound to the polynucleotide, immobilizing the polynucleotide-targeting element-separation group via the incorporated ddNTP (Column 7, lines 5-32; Column 9, lines 36-53 and Claim 18, steps a-g). Ju et al specifically teach the "entire sequencing reaction mixtures" are combined with streptavidin coated beads and the beads are immobilized. Following immobilization, the DNA fragments are removed (Column 7, lines 5-32 and Column 9, lines 36-53). This subsequent step of removing the DNA fragments is encompassed by the open claim language "comprising".

Regarding Claim 3, Ju et al disclose the method wherein the targeting element binds to the distinguishing element (i.e. adjacent to site of terminator incorporation, Column 5, lines 11-13),

Regarding Claim 4, Ju et al disclose the method wherein the targeting element comprises a nucleic acid sequence (i.e. primer, Column 5, lines 3-11).

Regarding Claim 5, Ju et al disclose the method wherein the targeting element comprises an oligonucleotide (i.e. primer, Column 5, lines 3-11).

Regarding Claim 6, Ju et al disclose the method wherein the targeting element comprises an extendable 3' hydroxy terminus (i.e. primer, Column 5, lines 3-11).

Regarding Claim 7, Ju et al disclose the method wherein the separation group is an immobilizable nucleotide i.e. biotinylated ddNTP (Column 6, lines 40-47).

Regarding Claim 8, Ju et al disclose the method wherein the separation group is an immobilizable nucleotide i.e. biotinylated ddNTP (Column 6, lines 40-47).

Regarding Claim 9, Ju et al disclose the method wherein the first separation group is attached to the targeting element by extending the oligonucleotide with a polymerase in the presence of biotinylated nucleotide forming an extended oligonucleotide containing immobilizable nucleotide (Column 6, lines 17-47).

Regarding Claim 10, Ju et al disclose the method wherein the targeting element comprises an oligonucleotide (i.e. primer, Column 5, lines 3-11).

Regarding Claim 11, Ju et al disclose the method wherein the separation group is an immobilizable nucleotide i.e. biotinylated ddNTP (Column 6, lines 40-47).

Regarding Claim 12, Ju et al disclose the method wherein the separation group is an immobilizable nucleotide i.e. biotinylated ddNTP (Column 6, lines 40-47).

Regarding Claim 13, Ju et al disclose the method wherein the population of molecules is DNA (Column 6, lines 17-22).

Regarding Claim 17, Ju et al disclose the method wherein the substrate is a particle, bead or magnetic bead (Column 7, lines 19-27).

Regarding Claim 18, Ju et al disclose the method further comprising contacting the population with a second targeting element simultaneously and capturing via a second separation group (Column 7, lines 5-32; Column 9, lines 36-53 and Claim 18, steps a-g).

Regarding Claim 39, Ju et al disclose a method for separating a polynucleotide molecule from a population comprising providing a population of nucleic acid molecules (i.e. mixture of differently sized primer extension products, Column 6, lines 13-47) comprising the polynucleotide having a first target sequence within 100 nucleotides of a distinguishing element (primer binding site adjacent to site of terminator incorporation, Column 5, lines 11-

13), contacting the population of nucleic acid molecules with a first targeting element (i.e. primer) which specifically binds to the polynucleotide molecule, selectively attaching a separation group comprising an immobilizable nucleotide (biotinylated ddNTP) to the targeting element bound to the polynucleotide wherein the attaching only occurs when the primer is bound to the polynucleotide, immobilizing the polynucleotide-targeting element-separation group via the incorporated ddNTP (Column 7, lines 5-32; Column 9, lines 36-53 and Claim 18, steps a-g).

Regarding Claim 40, Ju et al disclose the method wherein the oligonucleotide targeting element comprises an extendable 3' hydroxy terminus (i.e. primer, Column 5, lines 3-11).

Regarding Claim 41, Ju et al disclose the method wherein attachment of the separation group to the oligonucleotide is covalent (Column 6, lines 36-47).

Regarding Claim 42, Ju et al disclose the method wherein the first separation group is attached to the targeting element by extending the oligonucleotide with a polymerase in the presence of biotinylated nucleotide forming an extended oligonucleotide containing immobilizable nucleotide (Column 6, lines 17-47).

Regarding Claim 43, Ju et al disclose a method for separating a polynucleotide molecule from a population comprising providing a population of nucleic acid molecules (i.e. mixture of differently sized primer extension products, Column 6, lines 13-47) comprising the polynucleotide having a first target sequence within 100 nucleotides of a distinguishing element (primer binding site adjacent to site of terminator incorporation, Column 5, lines 11-13), contacting the population of nucleic acid molecules with a first targeting element (i.e. primer) which specifically binds to the polynucleotide molecule, selectively and covalently attaching a separation group comprising an immobilizable nucleotide (biotinylated ddNTP) to the targeting element bound to the polynucleotide wherein the attaching only occurs when the primer is bound to the polynucleotide, immobilizing the polynucleotide-targeting element-

separation group via the incorporated ddNTP (Column 7, lines 5-32; Column 9, lines 36-53 and Claim 18, steps a-g).

Regarding Claim 44, Ju et al disclose the method wherein the sequence of interest is an amplified sequence (Column 6, lines 17-31).

Regarding Claim 45, Ju et al disclose the method wherein the attachment occurs through ligation i.e. primer extension ligates nucleotides to the 3' hydroxyl (Column 6, lines 17-47). It is noted that the claim does not require a method step utilizing a specific ligase enzyme. As such, the ligation of the nucleotide onto the primer's 3' end is encompassed by the claimed ligation.

Regarding Claim 46, Ju et al disclose the method wherein covalent attachment occurs by polymerase extension (Column 6, lines 17-47).

5. Claims 1, 3-5, 10-13, 17, 21, 39, 50-52 and 55 are rejected under 35 U.S.C. 102(b) as being anticipated by Bukanov et al (Proc. Natl. Acad. Sci. USA, May 1998, 95: 5516-5520).

Regarding Claim 1, Bukanov et al disclose a method for separating a polynucleotide molecule from a population comprising providing a population of nucleic acid molecules (i.e. control and target plasmids, page 5517, left column) comprising the polynucleotide having a first target sequence (homopurine tracts) within 100 nucleotides of a distinguishing element (i.e. opposite strand, page 5517, Fig. 1 and page 5519, left column, third paragraph), contacting the population of nucleic acid molecules with a first targeting element (i.e. homopyrimidine probe) which specifically binds to the polynucleotide molecule, selectively attaching a separation group (biotinylated oligonucleotide probe) to the targeting element bound to the polynucleotide via the PD-loop structure wherein the attaching only occurs when

the probe is bound to the polynucleotide and immobilizing the polynucleotide-targeting element-separation group (page 5517-page 5518, left column).

Regarding Claim 3, Bukanov et al disclose the method wherein the targeting element binds within 20 nucleotides of the distinguishing element (i.e. on the opposite strand (page 5517, Fig. 1),

Regarding Claim 4, Bukanov et al disclose the method wherein the targeting element comprises a nucleic acid sequence (i.e. PNA opener, page 5516, right column).

Regarding Claim 5, Bukanov et al disclose the method wherein the targeting element comprises an oligonucleotide (i.e. . PNA oligomer, page 5516, right column).

Regarding Claim 10, Bukanov et al disclose the method wherein the targeting element comprises an oligonucleotide (i.e. . PNA oligomer, page 5516, right column).

Regarding Claim 11, Bukanov et al disclose the method wherein the separation group is an immobilizable nucleotide i.e. biotinylated oligo (page 5516, right column).

Regarding Claim 12, Bukanov et al disclose the method wherein the separation group is an immobilizable nucleotide i.e. biotinylated oligo (page 5516, right column).

Regarding Claim 13, Bukanov et al disclose the method wherein the population of molecules is DNA (page 5517, left column).

Regarding Claim 17, Bukanov et al disclose the method wherein the substrate is a particle, bead or magnetic bead (page 5517, left column).

Regarding Claim 21, Bukanov et al disclose the method wherein the DNA is genomic DNA (page 5517, left column).

Regarding Claim 39, Bukanov et al disclose a method for separating a polynucleotide molecule from a population comprising providing a population of nucleic acid molecules (i.e. control and target plasmids, page 5517, left column) comprising the polynucleotide having a first target sequence (homopurine tracts) within 100 nucleotides of a distinguishing element (i.e. opposite strand), contacting the population of nucleic acid molecules with a first targeting

element (i.e. homopyrimidine probe) which specifically binds to the polynucleotide molecule, selectively attaching a separation group (biotinylated oligonucleotide probe) to the targeting element bound to the polynucleotide via the PD-loop structure wherein the attaching only occurs when the probe is bound to the polynucleotide and immobilizing the polynucleotide-targeting element-separation group (page 5517-page 5518, left column).

Regarding Claim 50, Bukanov et al disclose a method for separating a polynucleotide molecule from a population comprising providing a population of nucleic acid molecules (i.e. control and target plasmids, page 5517, left column) comprising the polynucleotide having a first target sequence (homopurine tracts) within 100 nucleotides of a distinguishing element (i.e. opposite strand), contacting the population of nucleic acid molecules with a first targeting element containing a separation group (biotinylated oligonucleotide probe) which specifically binds to the polynucleotide molecule, selectively stabilizing the binding of the targeting element via PNA opener and immobilizing the polynucleotide-targeting element-separation group (page 5517-page 5518, left column).

Regarding Claim 51, Bukanov et al disclose the method wherein the targeting element is an oligonucleotide (page 5516, right column).

Regarding Claim 52, Bukanov et al disclose the method wherein the targeting element binds within 20 nucleotides of the distinguishing element (i.e. on the opposite strand (page 5517, Fig. 1 and page 5519, left column, third paragraph),

Regarding Claim 55, Bukanov et al disclose the method wherein the targeting element-separation group comprises a biotinylated nucleotide i.e. biotinylated oligo (page 5516, right column).

6. Claim 19 is rejected under 35 U.S.C. 102(e) as being anticipated by Engelhardt et al (U.S. Patent No. 6,221,581, filed 7 June 1995).

Regarding Claim 19, Engelhardt et al disclose a method for separating a polynucleotide molecule from a population comprising providing a population of nucleic acid molecules comprising the polynucleotide having a first target sequence within 100 nucleotides of a distinguishing element (e.g. mutation Column 12, lines 25-61), contacting the population of nucleic acid molecules with a first targeting element attached to a separation group (i.e. mutation-specific probe with a restriction enzyme site) which specifically binds to the polynucleotide molecule, selectively removing the separation group via digestion dependent upon presence or absence of the mutation and immobilizing the separation groups remaining attached to the separation group complex (Column 12, lines 25-61).

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 14-16, 21 and 47-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ju et al U.S. Patent No. 5,876,936, issued 2 March 1999) in view of Engelhardt et al (U.S. Patent No. 6,221,581, filed 7 June 1995).

Regarding Claims 14-16, 21 and 47-49, Ju et al disclose a method for separating a polynucleotide molecule from a population comprising providing a population of nucleic acid molecules (i.e. mixture of differently sized primer extension products, Column 6, lines 13-47) comprising the polynucleotide having a first target sequence within 100 nucleotides of a distinguishing element (primer binding site adjacent to site of terminator incorporation, Column 5, lines 11-13), contacting the population of nucleic acid molecules with a first targeting element (i.e. primer) which specifically binds to the polynucleotide molecule, selectively and covalently attaching a separation group comprising an immobilizable nucleotide (biotinylated ddNTP) to the targeting element bound to the polynucleotide wherein the attaching only occurs when the primer is bound to the polynucleotide, immobilizing the polynucleotide-targeting element-separation group via the incorporated ddNTP (Column 7, lines 5-32; Column 9, lines 36-53 and Claim 18, steps a-g).

Ju et al teach the method wherein the population comprises DNA molecules but they are silent regarding RNA or specific DNAs (e.g. cDNA or genomic DNA) or specific distinguishing elements (e.g. SNP). However, Engelhardt et al teach a similar method of separating a polynucleotide (Claims 112-116) wherein the DNA encompasses any DNA and they further teach the method is useful for detecting SNPs which clearly suggests that SNPs are important elements of genomic DNA (Column 2, lines 17-23; Column 3, lines 22-45; and Column 12, lines 26-50). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the SNP separation/detection of Engelhardt to the genomic DNA analysis of Ju et al based on the known importance of SNPs for the obvious benefits of separating and detecting important genomic DNA as suggested by Engelhardt (Column 2, lines 17-23).

9. Claims 53 and 54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bukanov et al (Proc. Natl. Acad. Sci. USA, May 1998, 95: 5516-5520) in view of Engelhardt et al (U.S. Patent No. 6,221,581, filed 7 June 1995).

Regarding Claims 53-54, Bukanov et al disclose a method for separating a polynucleotide molecule from a population comprising providing a population of nucleic acid molecules (i.e. control and target plasmids, page 5517, left column) comprising the polynucleotide having a first target sequence (homopurine tracts) within 100 nucleotides of a distinguishing element (i.e. opposite strand), contacting the population of nucleic acid molecules with a first targeting element containing a separation group (biotinylated oligonucleotide probe) which specifically binds to the polynucleotide molecule, selectively stabilizing the binding of the targeting element via PNA opener and immobilizing the polynucleotide-targeting element-separation group (page 5517-page 5518, left column). Bukanov et al teach the method wherein the polynucleotide of interest is genomic DNA page 5517, left column) and they teach their method has diagnostic applications (Abstract) but they do not teach specific diagnostic application e.g. detection of single nucleotide polymorphism (SNP).

Engelhardt et al teach a similar method of separating genomic DNA of interest and they further teach the method is useful for detecting SNPs which clearly suggests that SNPs are important elements of genomic DNA (Column 2, lines 17-23 and Column 12, lines 26-50). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the SNP separation/detection of Engelhardt to the genomic DNA analysis of Bukanov et al based on the known importance of SNPs for the obvious benefits of separating and detecting important genomic DNA as suggested by Engelhardt (Column 2, lines 17-23).

Conclusion

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (571) 272-0741. The examiner can normally be reached on 6:00 TO 3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

BJ Forman, Ph.D.
Primary Examiner
Art Unit: 1634
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